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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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207	7590	10/20/2004	EXAMINER	
WEINGARTEN, SCHURGIN, GAGNEBIN & LEOVICI LLP TEN POST OFFICE SQUARE BOSTON, MA 02109			YU, MISOOK	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/937,191

Applicant(s)

SCHUBERT, WALTER

Examiner

MISOOK YU, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-21 and 23-26 is/are pending in the application.
- 4a) Of the above claim(s) 9-15 and 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-8,16,21 and 23-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01/03/02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group 16 drawn to use of CD13 inhibitor in the reply filed on 26 July 2004 is acknowledged. The traversal is on the ground(s) that WO 98/44923 is about use of the aminopeptidase inhibitor actinonin for treating neoplastic cells in general while the amended instant claim 1 is drawn to usefulness of aminopeptidase inhibitor in treating the very early stages of tumor diseases. This is not found persuasive because:

PCT Rule 13.2 and 37 C.F.R. 1.475 define "special technical feature" as those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. The special technical feature of the instant first claim i.e. The main invention is at least one aminopeptidase inhibitor, does not contribute over the art because claim 1 anticipated by the art, fore example, WO 98/44923. Note the art rejection below with multiple references.

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; (2) A product and a process of use of said product; (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; (4) A process and an apparatus or means specifically designed for carrying out said

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process; or (5) A product, a process specially adapted for the manufacture of said product, and an apparatus or means specifically designed for carrying out said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).)

An inhibitor to each of the different proteins in claim 1 (total 30 different proteins) is a different product because they do not share common structures. Further Claims 9-15, 17-20 drawn to method of screening an inhibitor is not linked to form a single general inventive concept because they are drawn to finding (screening) an inhibitor to be utilized. In other words, the method in claims 9-15, and 17-20 does not fall into the single general inventive concept under PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). The requirement is still deemed proper and is therefore made FINAL.

Claims 9-15, and 17-20 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 26 July 2004.

Claims 1, 2, 4-21, and 23-26 are pending. Claims 1, 2, 4-8, 16, 21, and 23-26 are examined on merits as they are drawn to CD13 aminopeptidase inhibitor.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (e) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) BRIEF SUMMARY OF THE INVENTION.
- (g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (h) DETAILED DESCRIPTION OF THE INVENTION.
- (i) CLAIM OR CLAIMS (commencing on a separate sheet).
- (j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The instant specification has drawing but lacks BRIEF DESCRIPTION OF THE OF THE DRAWING(S). Appropriate correction is required.

Claim Objections

Claims 1, 2, 4-8, 16, 21, and 23-26 are objected to because of the following informalities: The claims have not been amended to reflect the election. Appropriate correction is required.

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Claims 4, and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The base claims that the instant claims depend on do not say anything about an inhibitor inhibiting at least one surface protein "that is not an aminopeptidase."

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 4-8, 16, 21, and 23-26 are rejected under 35 U.S.C. 101 because the claimed recitation of "Utilization" in the base claim 1, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8, 16, 21, and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The base claim 1 recites "Utilization of at least one aminopeptidase inhibitor for the production of a medicament" but it is not clear whether the instantly claimed invention is drawn to a process claim or product. If the claimed invention is drawn to a process, then the claims as currently construed lacks any active step, positive steps delimiting how the "utilization" is actually practiced. Since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

All claims depend on the rejected base claim are also rejected because the limitations of the base claims do not clear up the ambiguous and indefinite limitation in the base claims.

Further, claim 1 and all dependant claims are infinite because it is not clear what is being modified in the limitation "by modifying at least one surface protein CD13 as member of a protein network on the surface of the tumor cells whereby the protein network comprises up to 30 surface proteins" by the claimed "at least one aminopeptidase". Does the quoted limitation above mean that CD 13 in the network of up to 30 different protein is being modified by the claimed "at least one aminopeptidase"? It is confusing as to the scope of what is being modified by the claimed "at least one aminopeptidase"

Claims 1, 2, 4-8, 16, 21, and 23-26 are as a whole are confusing because of the limitation "at least one additional inhibitor". Claims 2, and 21 depend on claim 1, which is drawn to utilization of an inhibitor with the recited function. Claim 2 as currently

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construed appears to list several species that belong to the genus defined by its function in claim 1. However, claim 21 appears to say that the species listed in claim 2 do not belong to the genus of claim 1 but "at least one additional inhibitor". What is the relationship between the claimed inhibitor in claim 1 and the claimed inhibitors of claim 2. It is not clear whether homophthalimide, actinonin, bestatin, and an anti-CD13 monoclonal antibody would possess the function(s) recited in claim 1. In other words, it is not clear whether "blocking of polarization of invasive human or animal tumor cells by modifying at least one surface protein CD13 as member of a protein network on the surface of the tumor cells" is the characteristic of "homophthalimide", "actinonin", "bestatin", and an anti-CD13 monoclonal antibody. Claims 1, and 2 are drawn to utilization of at least one aminopeptidase but claim 21 is drawn to pharmaceutical comprising at least one aminopeptidase of claim 1 and "one additional inhibitor as claimed in claim 2". In claim 4, "at least one additional inhibitor" inhibits "at least one surface protein that is not an aminopeptidase". However, in claim 5, at least one aminopeptidase inhibitor and "at least one additional inhibitor" both have a same function. It appears that "at least one additional aminopeptidase" refers to at least two different entities; this in turn confuses the scope of the claimed invention.

Claims 8, 21, 23-26 are confusing because of the limitation "at least one additional inhibitor". The claims ultimately depend on claim 1, which does not say anything about "at least one additional inhibitor".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-8, 16, 21, and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There are two parts to this rejection.

First, this **new matter rejection** is made because the Office is unable to find the support for "very early stages of", and "wherein the treated tumor is a primary tumor" in the specification as originally filed. Applicant is kindly requested to point out the support for the limitations in the specification as originally filed.

Second, the **written description rejection** is made because the claimed invention is interpreted as drawn to genus of CD13 aminopeptidase inhibitors.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial

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structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, claims 1, 5-7 do not recite the complete or partial structure of the claimed inhibitor, nor do the claims provide physical and/or chemical properties, structure/function correlation, methods of making the claimed inhibitor. Only factor present in the claims are the functional characteristics of either at least one aminopeptidase or at least one additional peptidase". There is not even identification of any particular partial structure associated with the recited function. Claims 4, 16 neither specify the structure nor specify function of the claimed "at least one additional inhibitor". None of the specifically recited inhibitors in claim 2, i.e. homophthalimide type, actinonin, bestatin, an antibody to CD13 have a common structure although they appear to have a similar function, which indicates that in order to figure out how the other structures that meet the functional limitation of the base claim, one has to screen, for example using the method described in the instant specification. It is noted that law requires that the disclosure of an application shall inform those skilled in the art to disclose the structure of the product for the production of a medicament used in the treat, not how to screen it for themselves.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Claims 21, and 23-26 refer to claims 2, 4-7 respectively, therefore

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these claims fails to provide an adequate written description for the same reasons given for the base claims.

A definition by function alone “does not suffice, to sufficiently describe a coding sequence “because it is only an indication of what the gene does, rather than what it is.” *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406.

The specification at pages 12-14 teaches that a network of 30 cell surface proteins is involved in controlling polarization of tumor cells, and also teaches which surface proteins is being detected in Karpas (lymphoma derived) cells treated with actinonin at page 13. However, the specification does not teach, and Table 3 teaches combination of the surface protein in cells treated with certain surface proteins are how to screen for an compound that disrupts the protein network of up to

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, given that the specification has only described how to screen for the claimed genus of inhibitors. Therefore, only the art-known CD13 inhibitors i.e. homophthalimide, actinonin, bestatin, and an antibody to CD13, but not the full breadth of the claim meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 16, 21, and 23-26 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of WO 98 44923 (1998, IDS filed on 01/03/2002), Kagechika et al., (1999, Biol. Pharm. Bull., 22(9), 1010-1012, IDS filed on 01/03/2002), Xu et al., (Clin Cancer Res. 1998 Jan;4(1):171-6, IDS filed on 01/03/2002), or Fujii et al., (1996, Biol. Pharm. Bull. 19 (1), 6-10, IDS filed on 01/03/2002).

Claims 1-8, 16, 21, and 23-26 are broadly interpreted as drawn to a product and/or composition comprising at least one aminopeptidase inhibitor wherein said at least one aminopeptidase inhibitor is homophthalimide type and/or actinonin and/or bestatin, and/or an antibody to CD13, in particular a monoclonal antibody, against CD13 (note applicant's election), wherein claims 4-8, 16, 21, 23-26 has the limitation "an additional inhibitor".

The preamble recitation of "used in the treatment of very early stages of tumor diseases, wherein the treated tumor is a primary tumor" in claim 1, or "A pharmaceutical" in claims 8, 21, 23-26 are merely suggestive of an intended use and is not given patentable weight for purposes of comparing the claims with the prior art. The claims read on a product and/or composition *per se* comprising at least one aminopeptidase inhibitor, wherein said at least one aminopeptidase inhibitor is

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homophthalimide type and/or actinonin and/or bestatin, and/or an antibody to CD13, in particular a monoclonal antibody, against CD13.

WO 98 44923 teaches for example at page 2, at least one aminopeptidase inhibitor, wherein said at least one aminopeptidase inhibitor is homophthalimide type and/or actinonin and/or bestatin. The limitation "an additional inhibitor" is anticipated by the art because the art teaches more at least one inhibitor and "an additional inhibitor".

Kagechika et al., (1999, Biol. Pharm. Bull., 22(9), 1010-1012, IDS filed on 01/03/2002) teach at page 1010 the instantly claimed invention, i.e. at least one aminopeptidase inhibitor, wherein said at least one aminopeptidase inhibitor is homophthalimide type and/or actinonin and/or bestatin. The limitation "an additional inhibitor" is anticipated by the art because the art teaches more at least one inhibitor and "an additional inhibitor".

Xu et al., (Clin Cancer Res. 1998 Jan;4(1):171-6, IDS filed on 01/03/2002) teach i.e. at least one aminopeptidase inhibitor, wherein said at least one aminopeptidase inhibitor is homophthalimide type and/or actinonin and/or bestatin. The limitation "an additional inhibitor" is anticipated by the art because the art teaches more at least one inhibitor and "an additional inhibitor". Note the heading "Materials" at page 171, right column.

Fujii et al., (1996, Biol. Pharm. Bull. 19 (1), 6-10, IDS filed on 01/03/2002) also teach at least one aminopeptidase inhibitor, wherein said at least one aminopeptidase inhibitor is homophthalimide type and/or actinonin and/or bestatin. The limitation "an

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additional inhibitor" is anticipated by the art because the art teaches more at least one inhibitor and "an additional inhibitor". Note Table 1 at page 7.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



MISOOK YU, Ph.D.
Examiner
Art Unit 1642